UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,350	03/12/2004	Valery Krasnoperov	VASG-P01-002	2293

28120 7590 10/06/2005

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/800,350	KRASNOPEROV ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-62* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

NOTE: For restriction purposes, the claims were renumbered beginning with the second claim "23" (which was renumbered as claim "24").

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-11, 20, 22, and 24, drawn to an isolated soluble polypeptide comprising an amino acid sequence of an extracellular domain of an EphB4 protein, classified in class 530, subclass 350.

(Upon election of Group I, Applicant must select <u>one</u> sequence from Figure 65, Figure 1, <u>or</u> Figure 2, as each represents a separate invention and not a separate species. Any claims not reading on the elected sequence will be withdrawn as being drawn to a non-elected invention.)

II. Claims 12-19, 21, 23, and 25, drawn to an isolated soluble polypeptide comprising an amino acid sequence of an extracellular domain of an Ephrin B2 protein, classified in class 530, subclass 350.

(Upon election of Group II, Applicant must select <u>one</u> sequence from Figure 66 <u>or</u> Figure 3, as each represents a separate invention and not a separate species. Any claims not reading on the elected sequence will be withdrawn as being drawn to a non-elected invention.)

III. Claims 26-34, as specifically drawn to an antagonist antibody which binds to an extracellular domain of an *EphB4 protein* and inhibits an activity of EphB4, classified in class 530, subclass 387.1.

IV. Claims 26-34, as specifically drawn to an antagonist antibody which binds to an extracellular domain of an *Ephrin B2 protein* and inhibits an activity of Ephrin B2, classified in class 530, subclass 387.1.

V. Claims 35, 38-56, 59, and 60, as specifically drawn to a method of treating a tumor, inhibiting angiogenesis, and inhibiting signaling through the Ephrin B2/EphB4 pathway in a cell comprising contacting the cell with a soluble polypeptide of Group I, classified in class 514, subclass 2. **(Upon election of Group V, Applicant must specifically identify <u>one</u> polypeptide as delineated in Group I above, as each represents a separate invention and not a separate species. Any claims not reading on the elected sequence will be withdrawn as being drawn to a non-elected invention.)**

VI. Claims 36-56, 59, and 60, as specifically drawn to a method of treating a tumor, inhibiting angiogenesis, and inhibiting signaling through the Ephrin

B2/EphB4 pathway in a cell comprising contacting the cell with a soluble polypeptide of Group II, classified in class 514, subclass 2.

(Upon election of Group VI, Applicant must select <u>one</u> sequence as each represents a separate invention and not a separate species. Any claims not reading on the elected sequence will be withdrawn as being drawn to a non-elected invention.)

VII. Claim 38-39, 40-52, 53-56, 59, and 60, as specifically drawn to a method of inhibiting angiogenesis and treating a tumor or a patient suffering from cancer comprising administering an antibody from Group III, classified in class 424, subclass 130.1.

(Upon election of Group VII, Applicant must select <u>one</u> sequence as each represents a separate invention and not a separate species. Any claims not reading on the elected sequence will be withdrawn as being drawn to a non-elected invention.)

VIII. Claim 38-39, 40-52, 53-56, 59, and 60, as specifically drawn to a method of inhibiting angiogenesis and treating a tumor or a patient suffering from cancer comprising administering an antibody from Group IV, classified in class 424, subclass 130.1.

(Upon election of Group VIII, Applicant must select <u>one</u> sequence as each represents a separate invention and not a separate species.

Any claims not reading on the elected sequence will be withdrawn as being drawn to a non-elected invention.)

IX. Claims 57-58, as specifically drawn to use of a polypeptide from Group I in the manufacture of a medicament, classified in class 514, subclass 2. **(Upon election of Group IX, Applicant must select <u>one</u> sequence as each represents a separate invention and not a separate species. Any claims not reading on the elected sequence will be withdrawn as being drawn to a non-elected invention.)**

X. Claims 57-58, as specifically drawn to use of a polypeptide from Group II in the manufacture of a medicament, classified in class 514, subclass 2. **(Upon election of Group X, Applicant must select <u>one</u> sequence as each represents a separate invention and not a separate species. Any claims not reading on the elected sequence will be withdrawn as being drawn to a non-elected invention.)**

XI. Claims 57-58, as specifically drawn to use of an antibody from Group III in the manufacture of a medicament, classified in class 530, subclass 387.1.

XII. Claims 57-58, as specifically drawn to use of use of an antibody from Group IV in the manufacture of a medicament, classified in class 530, subclass 387.1.

XIII. Claim 61-62, as specifically drawn to a method for identifying a tumor that is suitable for treatment with an EphrinB2 or EphB4 antagonist comprising detecting the expression of EphB4 protein, classified in class 435, subclass 7.1.

XIV. Claim 61-62, as specifically drawn to a method for identifying a tumor that is suitable for treatment with an EphrinB2 or EphB4 antagonist comprising detecting the expression of EphB4 mRNA, classified in class 435, subclass 6.

XV. Claims 61-62, as specifically drawn to a method for identifying a tumor that is suitable for treatment with an EphrinB2 or EphB4 antagonist comprising detecting the expression of Ephrin B2 protein, classified in class 435, subclass 7.1.

XVI. Claims 61-62, as specifically drawn to a method for identifying a tumor that is suitable for treatment with an EphrinB2 or EphB4 antagonist

comprising detecting the expression of Ephrin B2 mRNA, classified in class 435, subclass 6.

XVII. Claims 61-62, as specifically drawn to a method for identifying a tumor that is suitable for treatment with an EphrinB2 or EphB4 antagonist comprising detecting the gene amplification of the EphB4 gene, classified in class 435, subclass 6.

XVIII. Claims 61-62, as specifically drawn to a method for identifying a tumor that is suitable for treatment with an EphrinB2 or EphB4 antagonist comprising detecting the gene amplification of the EphrinB2 gene, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

The inventions of Groups I-IV represent separate and distinct products. Group I is drawn to an EphB4 polypeptide, Group II is drawn to an Ephrin B2 polypeptide, Group III is drawn to an antibody which binds EphB4, and Group IV is drawn to an antibody which binds Ephrin B2. These products are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. The polypeptides of Groups I-II and the antibodies of Groups III-IV are patentably distinct for the following reasons:

While the inventions of Groups I-IV are all polypeptides, in this instance the polypeptide of Group I represents a purified EphB4 polypeptide and the polypeptide of Group II represents a purified Ephrin B2 polypeptide, while the polypeptide of Group III-IV encompasses antibodies including IgG which comprises 2 heavy and 2 light chains containing constant and variable regions, and including framework regions which act as a scaffold for the 6 complementarily determining regions (CDR) that function to bind an epitope. Thus the polypeptides of Groups I-II and the antibodies of Groups III-IV are structurally distinct molecules; any relationship between a polypeptide of Groups I-II and an antibodies of Groups III-IV is dependent upon the correlation between the scope of the polypeptide that the antibody binds and the scope of the antibodies that would be generated upon immunization with the polypeptide. In this case, the polypeptides of Groups I-II contains potentially hundreds of regions to which an antibody may bind, whereas the antibodies of Groups III-IV are defined in terms of binding specificity to a small structure. Furthermore, searching the inventions of Groups I-IV would impose a serious search burden. The inventions have separate status in the art as shown by their different classifications. A polypeptide and an antibody which binds to the polypeptide require different searches. An amino acid sequence search of the full-length protein is necessary for a determination of novelty and unobviousness of the protein. However, such a search is not required to identify the antibody of Group III. Furthermore, antibody which binds to an epitope of a polypeptide of Groups I-II may be known even if a polypeptides of Groups I-II are novel. In addition, the technical

literature search for the polypeptides of Groups I-II and the antibodies of Groups III-IV are not coextensive, e.g., antibodies may be characterized in the technical literature prior to discovery of or sequence of their binding target.

The inventions of Groups V-XVIII are materially distinct methods. Group V is drawn to a method comprising contacting a cell with an EphB4 polypeptide, Group VI is drawn to a method comprising contacting a cell with an Ephrin B2 polypeptide, Group VII is drawn to a method comprising administering an antibody which binds EphB4, Group VIII is drawn to a method comprising administering an antibody which binds Ephrin B2, Group IX is drawn to a method comprising use of an EphB4 polypeptide in the manufacture of a medicament, Group X is drawn to a method comprising use of an Ephrin B2 polypeptide in the manufacture of a medicament, Group XI is drawn to a method comprising use of an antibody which binds EphB4 in the manufacture of a medicament, Group XII is drawn to a method comprising use of an antibody which binds an Ephrin B2 polypeptide in the manufacture of a medicament, Group XIII is drawn to a method comprising detecting the expression of EphB4 protein, Group XIV is drawn to a method comprising detecting the expression of EphB4 mRNA, Group XV is drawn to a method comprising detecting the expression of Ephrin B2 protein, Group XVI is drawn to a method comprising detecting the expression of Ephrin B2 mRNA, Group XVII is drawn to a method comprising detecting the gene amplification of the EphB4 gene, and Group XVIII is drawn to a method comprising detecting the amplification of the Ephrin

B2 gene. These methods differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success.

Inventions I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide can be used in the materially different process of generating antibodies.

Inventions II and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide can be used in the materially different process of generating antibodies.

Inventions III and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different

process of using that product (MPEP § 806.05(h)). In the instant case the antibody can be used in the materially different process of screening for EphB4 expression.

Inventions IV and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody can be used in the materially different process of screening for Ephrin B2 expression.

Inventions I and IX are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide can be used in the materially different process of generating antibodies.

Inventions II and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different

process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide can be used in the materially different process of generating antibodies.

Inventions III and XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody can be used in the materially different process of screening for EphB4 expression.

Inventions IV and XII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody can be used in the materially different process of screening for Ephrin B2 expression.

Inventions III and XIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different

process of using that product (MPEP § 806.05(h)). In the instant case the antibody can be used in the materially different process of inhibiting angiogenesis.

Inventions IV and XV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody can be used in the materially different process of inhibiting angiogenesis.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Note:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for

patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Species

This application contains claims directed to the following patentably distinct species of the claimed invention:

The diseases listed in **claims 43 and 55** are listings of distinct **species of cancers**. Each species represent separate and distinct cell types with different morphologies and functions such that one species could not be interchanged with the other. Further, the above species are distinct diseases which differ at least in etiology, pathology, and mechanisms. As such, each species requires different searches and the consideration of different patentability issues.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

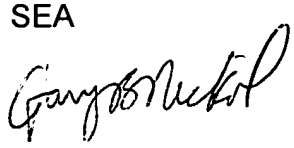
Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA



GARY B. NICKOL, PH.D.
PRIMARY EXAMINER